Risk Factors for Type 2 Diabetes Mellitus in Middle Age

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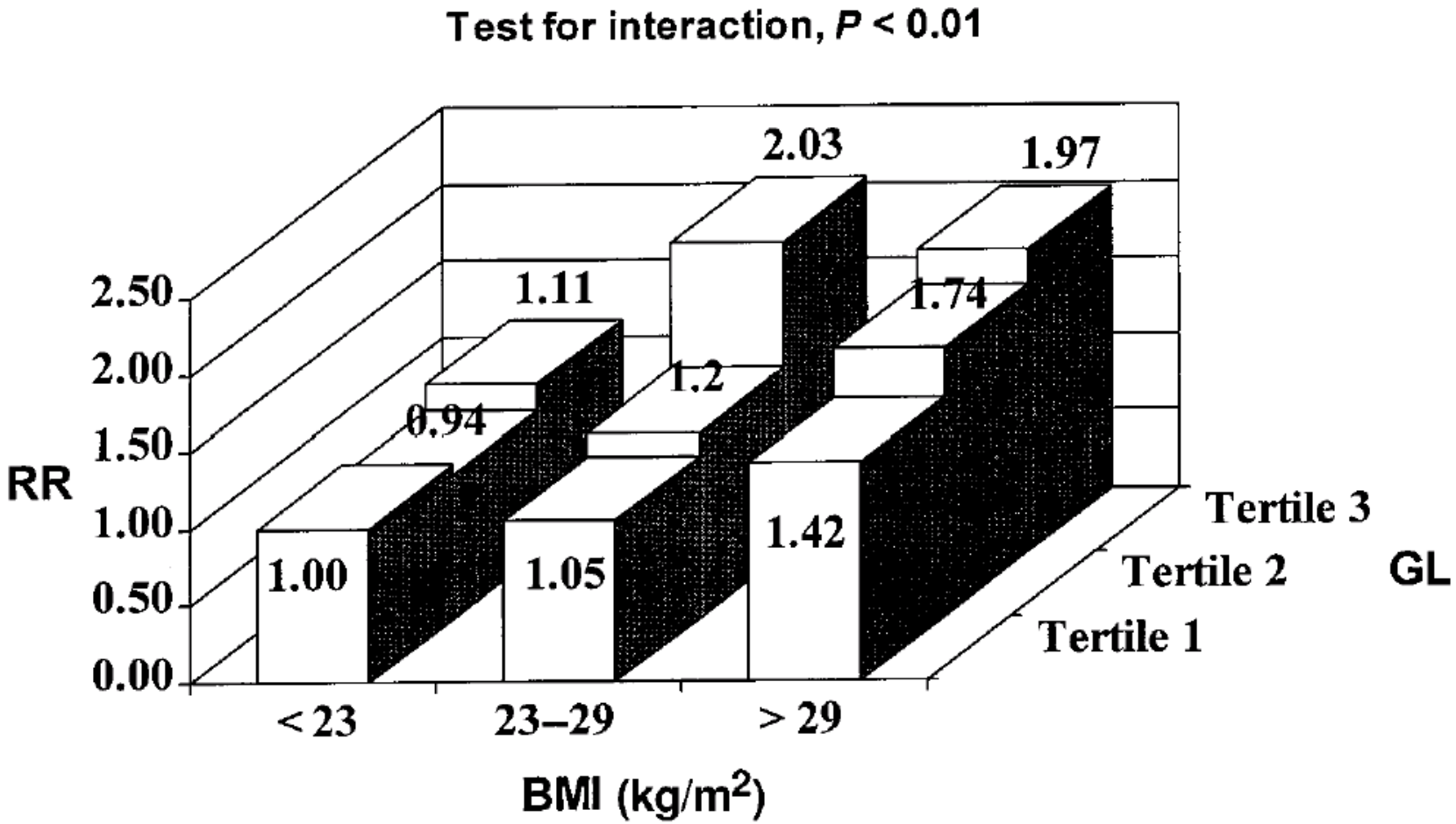
Risk Factors for Type 2 Diabetes

Osler's Principles & Practice of Medicine, 1892

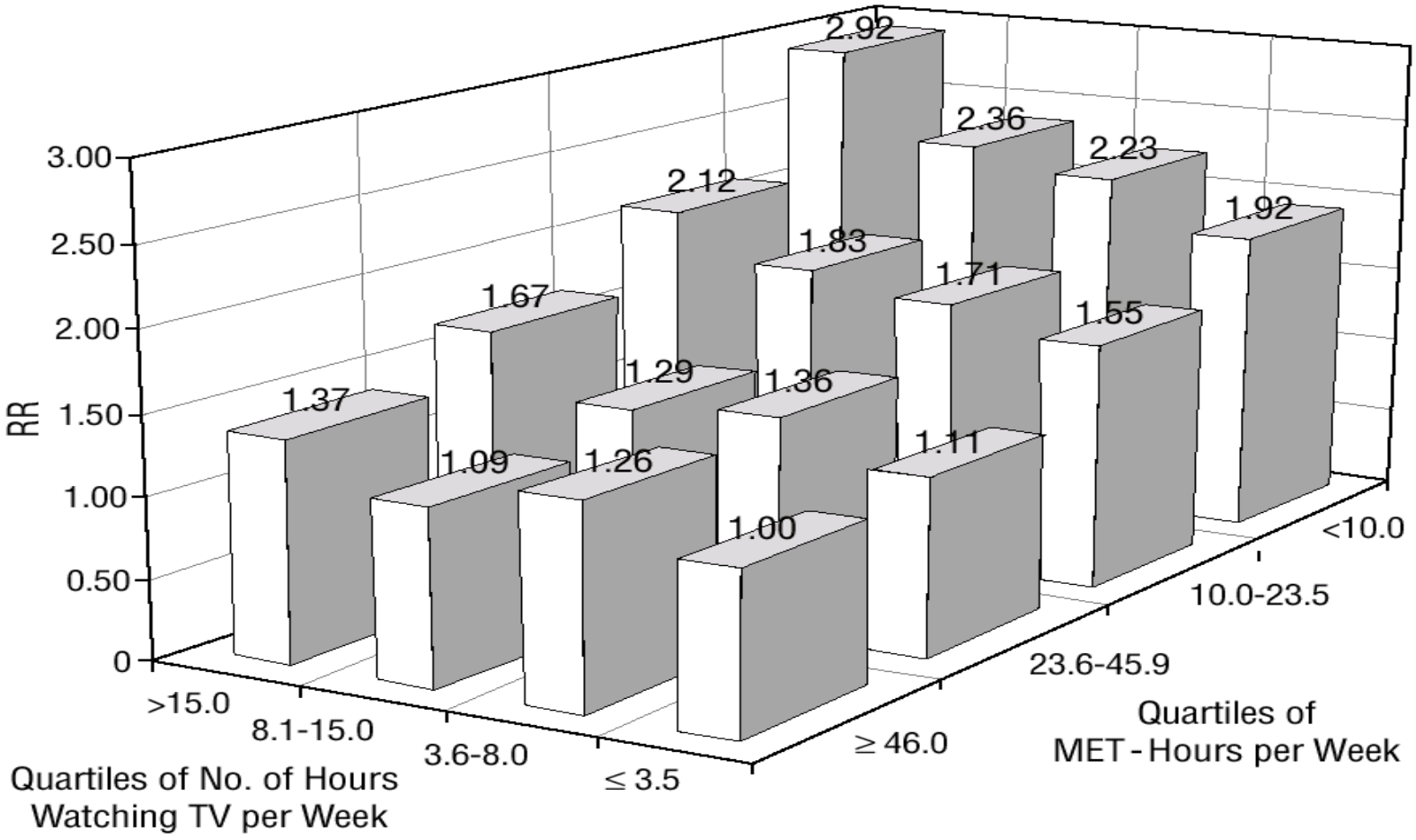
- Heredity
- Ethnicity
- Social Class
- Adiposity
- Sedentary life
- Overindulgence
- Defective Assimilation
- Nervous strain
- Worry
- CNS Lesions
- Environment
- Infections
- Liver Disturbances

Adjusted Relative Risk of Incident CHD by Body-Mass Index and Dietary Glycemic Load in 75,521 Women: The Nurses Health Study



S Liu et al. Amer J Clin Nutr 2000; 1455-61

Relative Risk of Diabetes in 37,918 Middle-Aged Male Clinicians by Physical Activity and TV Time



FB Hu et al. Arch Inter Med 2001; 161:1542-48.

Adjusted Relative Hazard (per Interquartile Range) of Incident Type 2 Diabetes in Middle Aged Adults by Vital Exhaustion Depression Subscore: The ARIC Study

Vital exhaustion depression subscore category*	Age, race, ARIC center, education, and sex adjusted hazard ratio (95% CI)†	Fully adjusted model (95% CI)‡
Vegetative score	1.22 (1.11–1.36)§	1.10 (0.99–1.23)
Nonvegetative score	1.20 (1.09–1.32)§	1.09 (0.98–1.20)
Functional score	1.23 (1.11–1.36)§	1.11 (1.00–1.23)§

*Vegetative symptoms (fatigue, sleep pattern, energy, concentration); nonvegetative symptoms (crying spells, hopelessness, irritability, enjoyment of sex, suicidality); functional symptoms (coping, productivity). †Risk of incident diabetes per interquartile range increase in vital exhaustion depression subscore category (each hazard ratio has been standardized to the interquartile range for the distribution of its scores). ‡Adjusted for age, race, ARIC center, education, sex, fasting insulin, fasting glucose, log triglycerides, HDL, BMI, waist-to-hip ratio, systolic BP, physical activity, total caloric intake, and smoking status. §*P* 0.05.

SH Golden et al. Diabetes Care 27:429–435, 2004

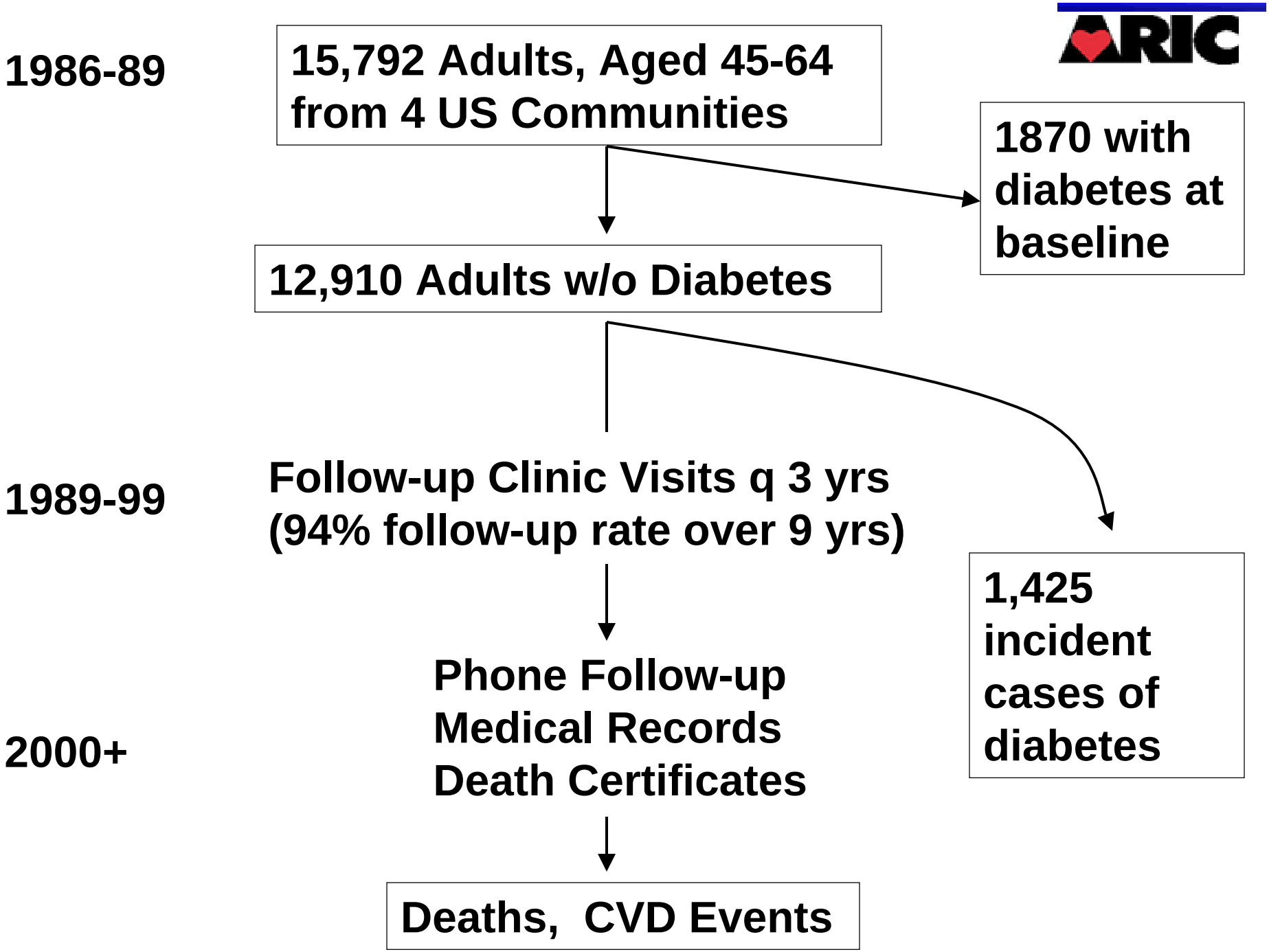
Atherosclerosis Risk in Communities Study

15,000 Adults Aged 45-64 at Baseline from 4 US Communities

1986-89	Visit 1	Carotid Ultrasound, PFTs, Bank Serum & DNA
1990-92	Visit 2	Carotid Ultrasound, PFTs
1993-95	Visit 3	Retinal Photos, Echocardiograms
1996-98	Visit 4	OGTT, Microalbuminuria
1999-	*Follow-up for Deaths, Hospitalizations*	
2004-2006	Visit 5	More DNA; Carotid MRI

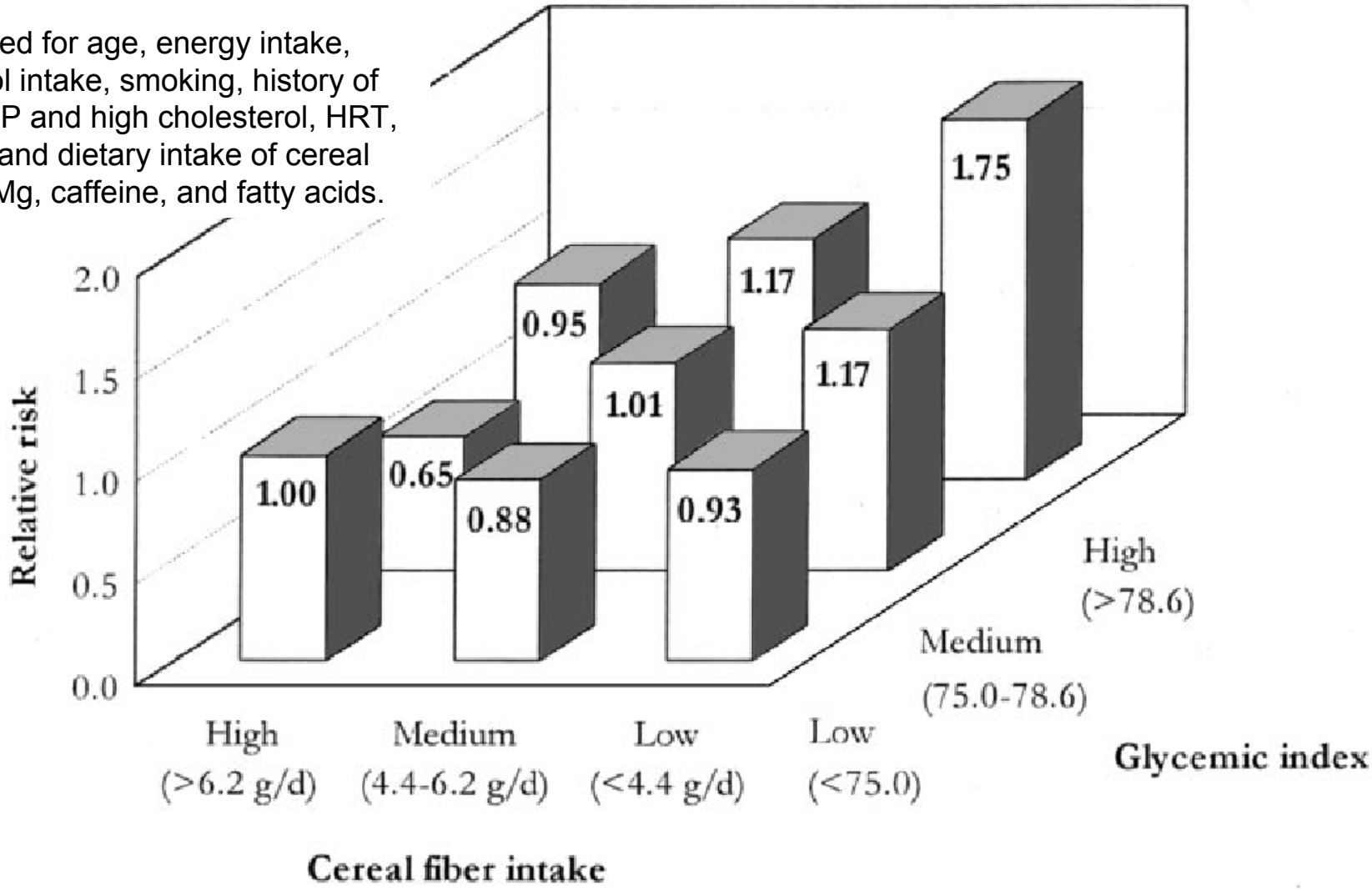
At all visits: Fasting labs, Anthropometry, BP, Diet, Health Behaviors

Funded by NHLBI (N01) Coresh, Hopkins PI


1986-89
15,792 Adults, Aged 45-64
from 4 US Communities
1870 with
diabetes at
baseline
12,910 Adults w/o Diabetes
1989-99
Follow-up Clinic Visits q 3 yrs
(94% follow-up rate over 9 yrs)
1,425
incident
cases of
diabetes
2000+
Phone Follow-up
Medical Records
Death Certificates
Deaths, CVD Events

Relative Risk of Incident Type 2 Diabetes in 91,249 Women by Levels of Cereal Fiber Intake and Dietary Glycemic Index

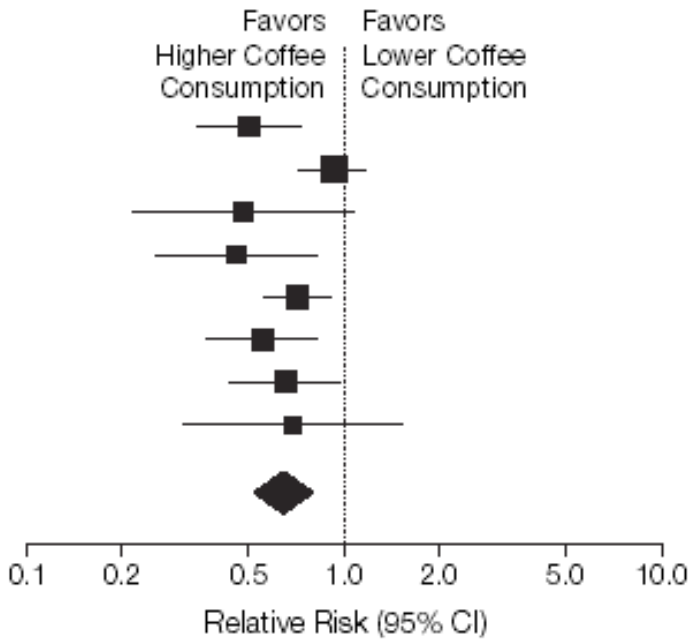
Adjusted for age, energy intake, alcohol intake, smoking, history of high BP and high cholesterol, HRT, OCP, and dietary intake of cereal fiber, Mg, caffeine, and fatty acids.



Relative Risk of Incident Type 2 Diabetes by Level of Coffee Consumption (Highest vs Lowest) in Adults: A Meta-Analysis of 8 Published Studies

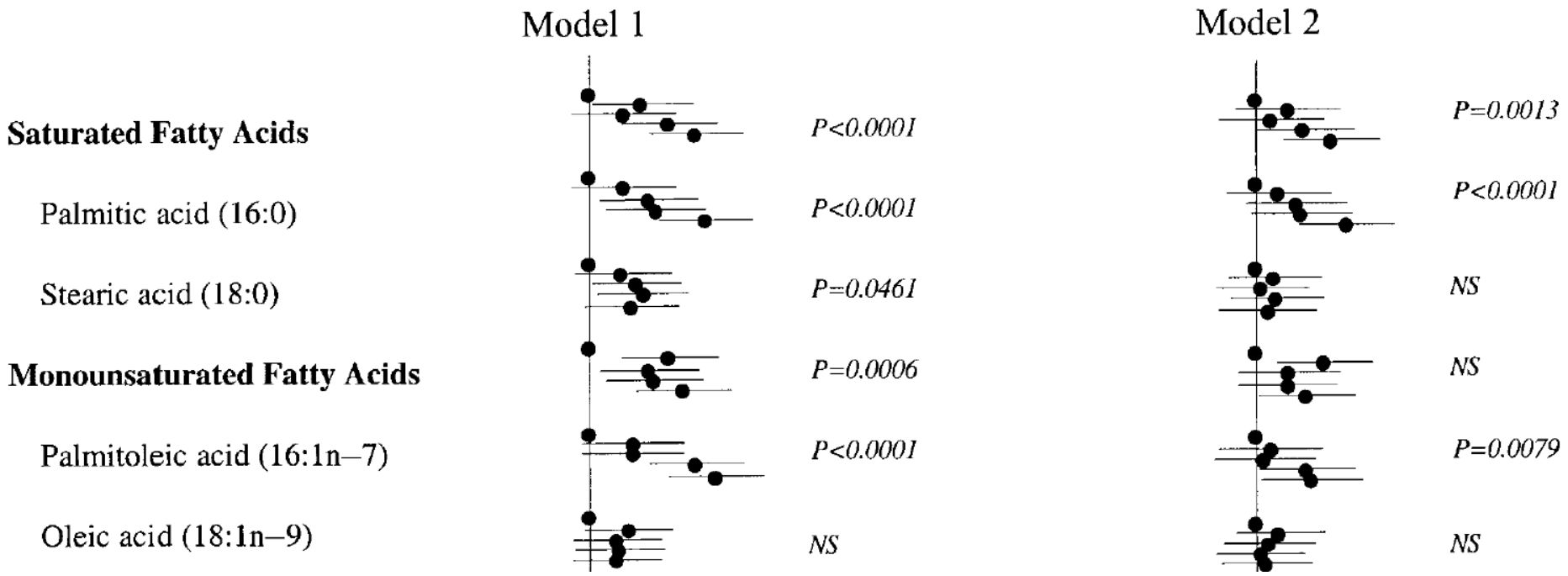
Highest vs Lowest Coffee Consumption

Source	Coffee Consumption, No. of Cups/d: Highest	Coffee Consumption, No. of Cups/d: Lowest (Referent)	Relative Risk (95% CI)
Van Dam and Feskens,[21] 2002	≥7	≤2	0.50 (0.35-0.72)
Reunanen et al,[27] 2003	≥7	≤2	0.92 (0.73-1.16)
Rosengren et al,[22] 2004	≥7	≤2	0.48 (0.22-1.06)
Salazar-Martinez et al,[25] 2004 (Males)	≥6	0	0.46 (0.26-0.82)
Salazar-Martinez et al,[25] 2004 (Females)	≥6	0	0.71 (0.56-0.89)
Tuomilehto et al,[23] 2004	7-9	≤2	0.55 (0.37-0.81)
Carlsson et al,[24] 2004	≥7	≤2	0.65 (0.44-0.96)
Van Dam et al,[30] 2004	≥7	≤2	0.69 (0.31-1.51)
Total (95% CI)			0.65 (0.54-0.78)



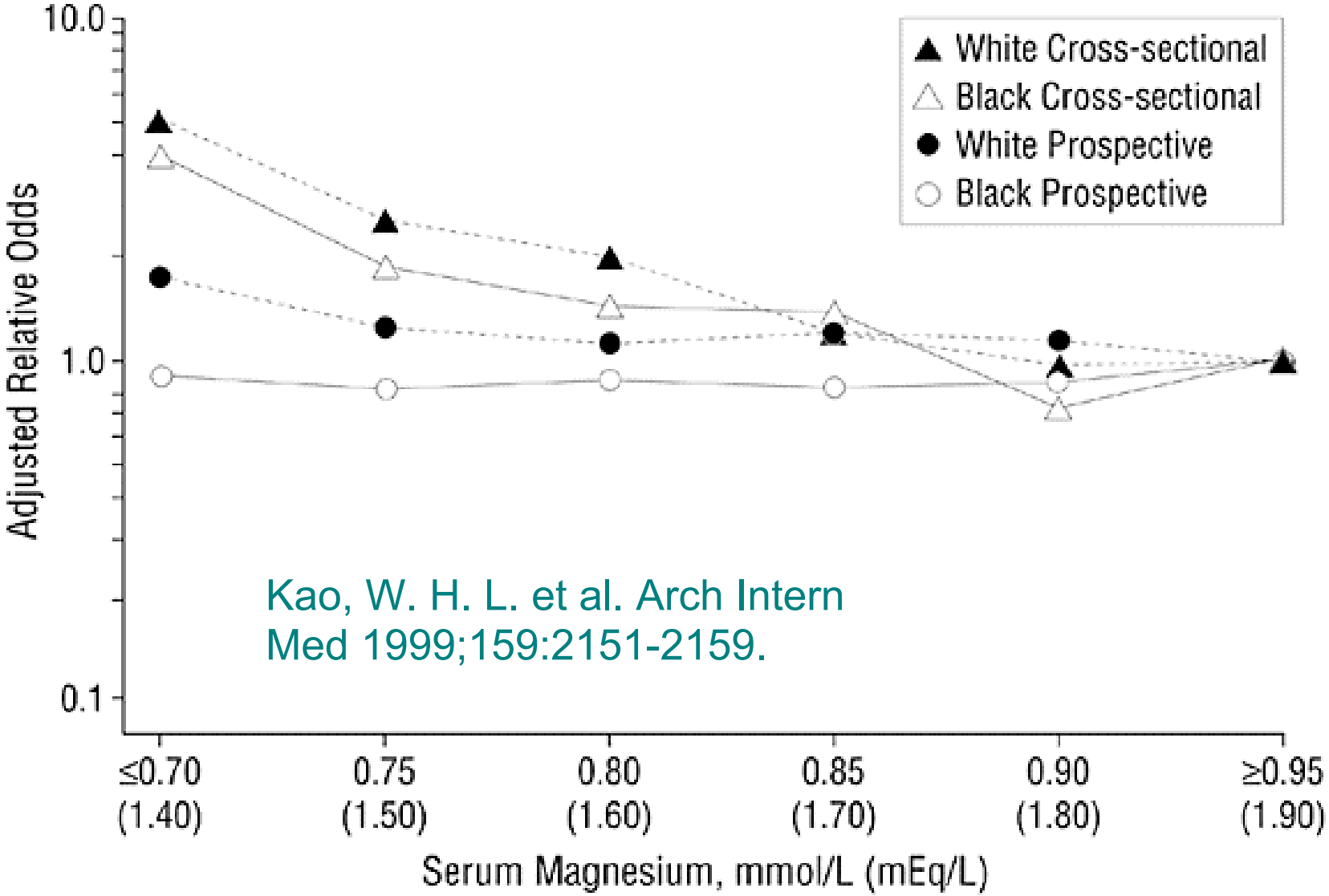
RM vanDam et al. JAMA. 2005;294:97-104

Relative Risk of Incident Type 2 Diabetes by Baseline Serum Levels of Saturated and Monounsaturated Fatty Acids in 2909 Middle Aged ARIC Participants, Minnesota Site



L Wang et al. Am J Clin Nutr 2003;78:91–8.

Incident Type 2 Diabetes in 12,128 Middle Aged Adults by Serum Mg and Race: The ARIC Study



Kao, W. H. L. et al. Arch Intern Med 1999;159:2151-2159.

Relative Risk of Incident Type 2 Diabetes in 6,838 Middle Aged Women by Alcohol Consumption: The ARIC Study

Alcohol consumption (drinks/week)	Women		
	Model 1†	Model 2‡	Model 3§
>21	0.41 (0.10, 1.77)	0.52 (0.12, 2.26)	0.33 (0.08, 1.48)
14.1–21	0.64 (0.25, 1.64)	0.77 (0.29, 2.00)	0.54 (0.20, 1.43)
7.1–14	0.81 (0.47, 1.37)	0.88 (0.52, 1.51)	0.63 (0.36, 1.11)
1.1–7	1.09 (0.80, 1.49)	1.14 (0.84, 1.56)	0.98 (0.71, 1.36)
≤1	1.00 (reference)	1.00 (reference)	1.00 (reference)
Former drinkers	1.10 (0.81, 1.49)	1.09 (0.79, 1.48)	1.18 (0.85, 1.65)
Lifetime abstainers	1.10 (0.84, 1.43)	1.08 (0.82, 1.43)	1.15 (0.86, 1.54)
p for overall¶	0.53	0.82	0.10
p for trend#	0.11	0.35	0.02

† Model 1 adjusted for age, race, education, family history of diabetes, BMI, waist/hip ratio, physical activity, total energy intake, smoking, and history of hypertension

‡ Model 2 = model 1 + fasting serum insulin; § Model 3 = model 2 + fasting serum glucose

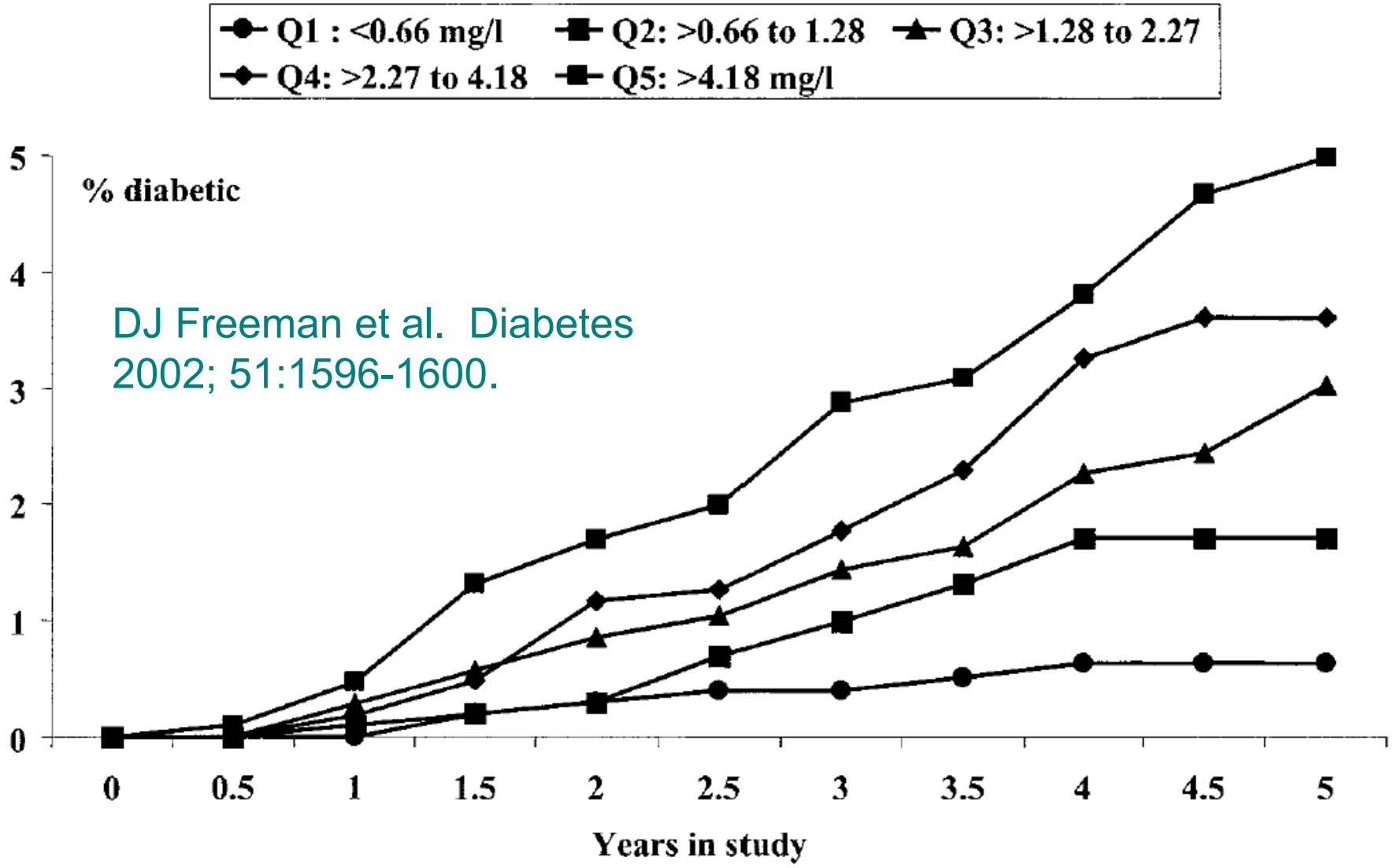
Relative Risk of Type 2 Diabetes in 21,068 Male Physicians by History of Cigarette Smoking

Pack-Years of Smoking	Cases	Age-Adjusted*	Multivariate Adjusted†
0 (never smoker)	323	1.0 (Referent)	1.0 (Referent)
1 to 19.9	148	1.0 (0.8–1.2)	1.0 (0.8–1.3)
20 to 39.9	116	1.4 (1.1–1.7)	1.3 (1.0–1.6)
≥40	122	2.1 (1.7–2.5)	1.6 (1.3–2.1)
P for trend‡		<0.001	<0.001

Multivariate model includes age, BMI, physical activity, hypertension, high cholesterol, family history of premature MI, alcohol consumption, and trial group (ASA vs carotene)

JE Manson et al. Amer J Med 2000; 109:538-542

Cumulative Incidence of Type 2 Diabetes in 5,974 Scottish Men by Quintile of C-Reactive Protein at Baseline



DJ Freeman et al. Diabetes 2002; 51:1596-1600.

Relative Odds of Incident Diabetes in 12,330 Adults by Selected Inflammatory Makers: The ARIC Study

Marker	Model 1*	Model 2†
High white-cell count		
Diabetes definition 1‡	1·9 (1·6–2·3)	1·5 (1·3–1·8)
Diabetes definition 2§	2·1 (1·6–2·6)	1·6 (1·3–2·0)
Low serum albumin		
Diabetes definition 1‡	1·3 (1·0–1·5)	0·98 (0·80–1·2)
Diabetes definition 2§	1·4 (1·1–1·7)	1·1 (0·85–1·4)
High fibrinogen		
Diabetes definition 1‡	1·2 (1·0–1·5)	0·93 (0·77–1·1)
Diabetes definition 2§	1·3 (1·1–1·7)	1·0 (0·79–1·2)

*Adjusted for age, sex, centre, ethnic origin, baseline glucose, family history of diabetes, physical activity, and pack-years of cigarette smoking. †Adjusted additionally for body-mass index and waist-to-hip ratio. ‡Fasting glucose cut-off value 7·0 mmol/L. §Fasting glucose cut-off value 7·8 mmol/L.

MI Schmidt et al. Lancet 1999; 353:1649-52.

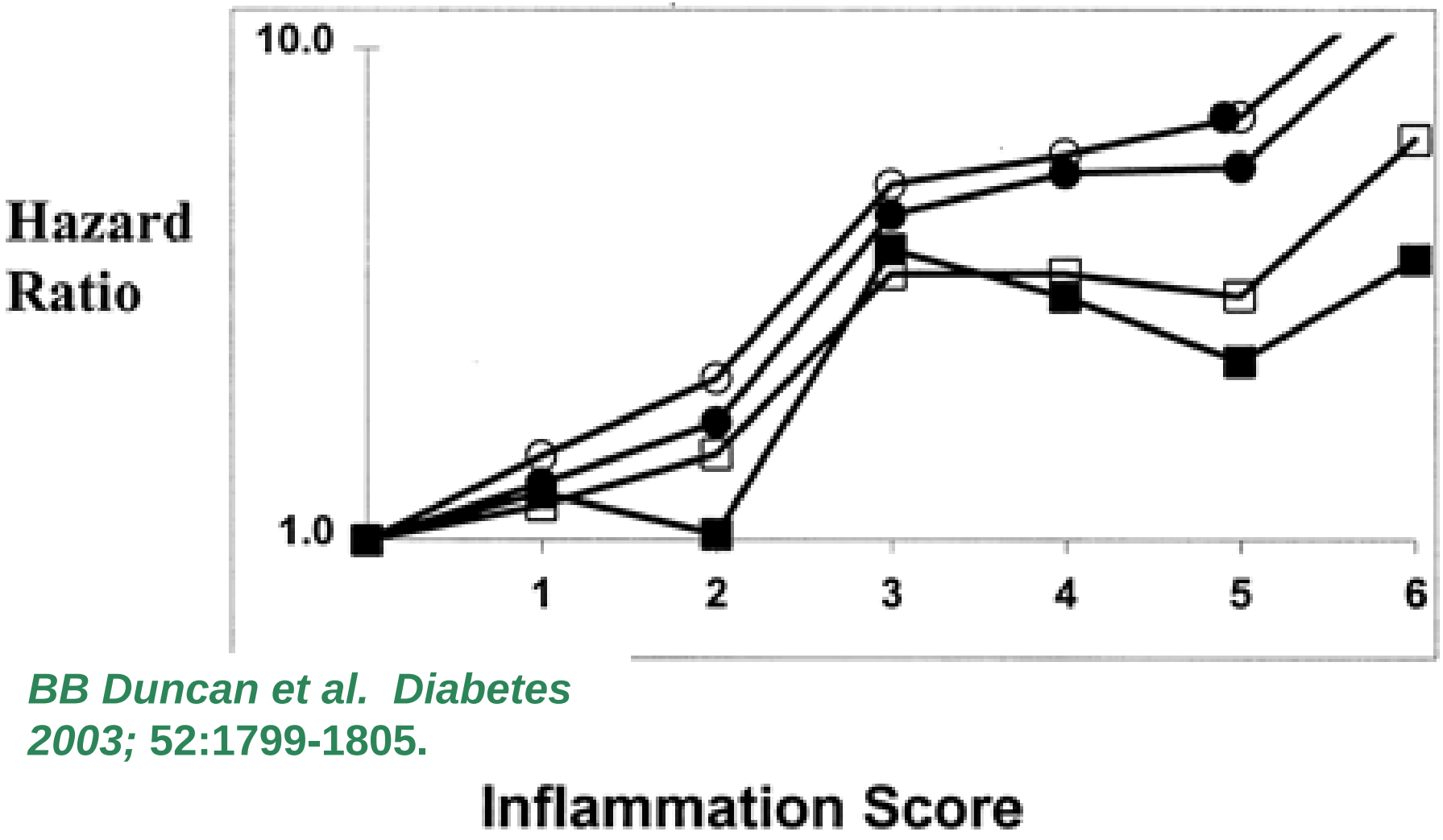
Relative Odds of Incident Diabetes in 610 Adults by Selected Inflammatory Makers: The ARIC Study

Marker	Model 1* (odds ratio [95% CI])	Model 2 (odds ratio [95% CI])†	
		All cases	First 3 years‡
Sialic acid	3·7 (1·4–9·8)	2·8 (1·0–8·1)	4·4 (1·1–16·8)
Orosomucoid	7·9 (2·6–23·7)	7·1 (2·1–23·7)	7·9 (1·9–32·3)
α_1-antitrypsin	1·0 (0·4–2·4)	1·1 (0·4–2·8)	1·8 (0·6–4·9)
Haptoglobin	1·7 (0·7–4·0)	1·6 (0·6–4·1)	2·1 (0·7–6·0)

*Adjusted for age, sex, ethnic origin, atherosclerosis case-control status, fasting plasma glucose, family history of diabetes, and smoking status. †Adjusted additionally for body-mass index and waist-to-hip ratio. ‡Analysis only of diabetes detected at visit three.

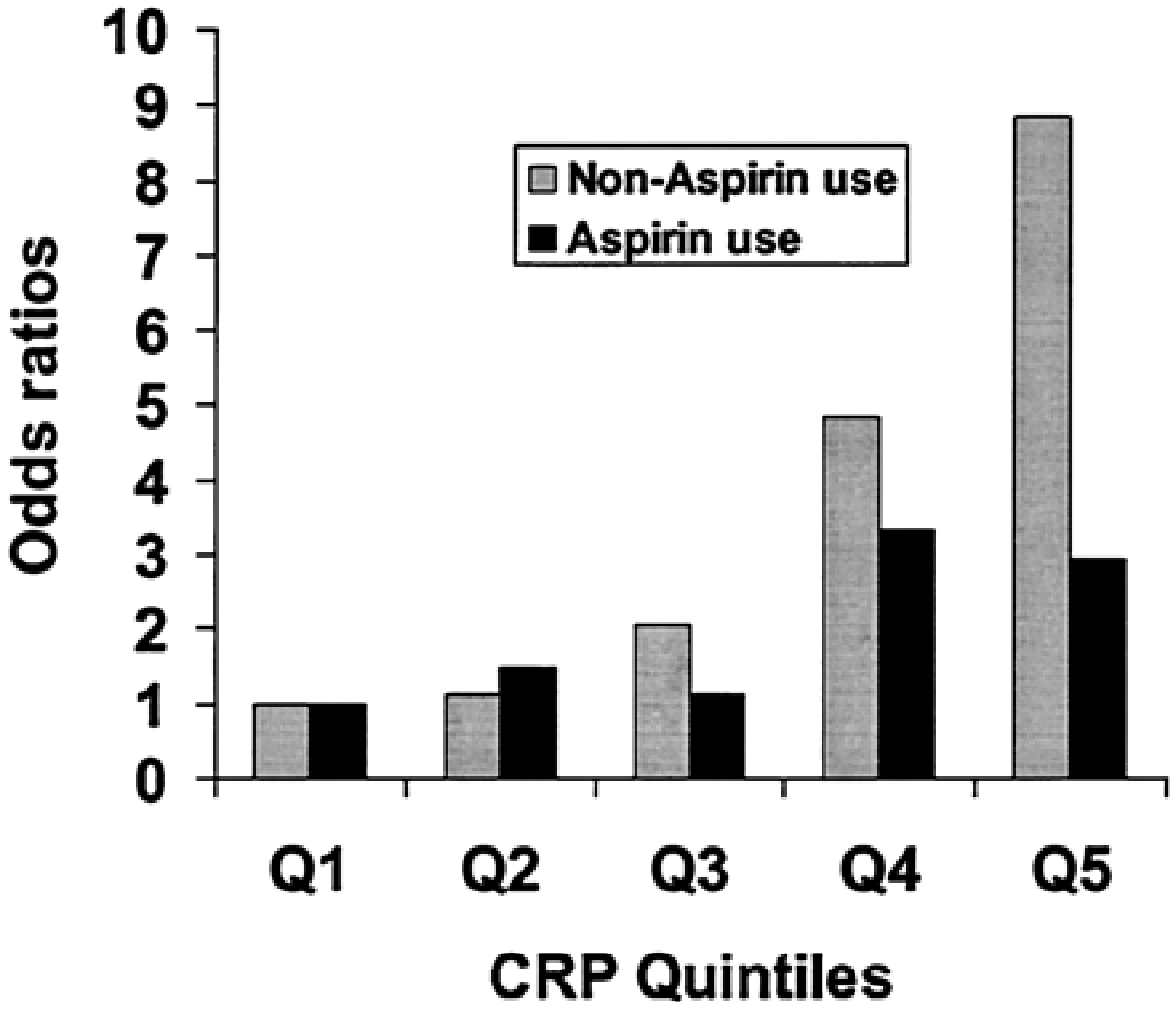
MI Schmidt et al. Lancet 1999; 353:1649-52.

Adjusted Relative Hazard of Incident Type 2 Diabetes by Inflammation Score in White, Non-Smoking Adults, Aged 45-64: ARIC Study



BB Duncan et al. Diabetes 2003; **52:1799-1805.**

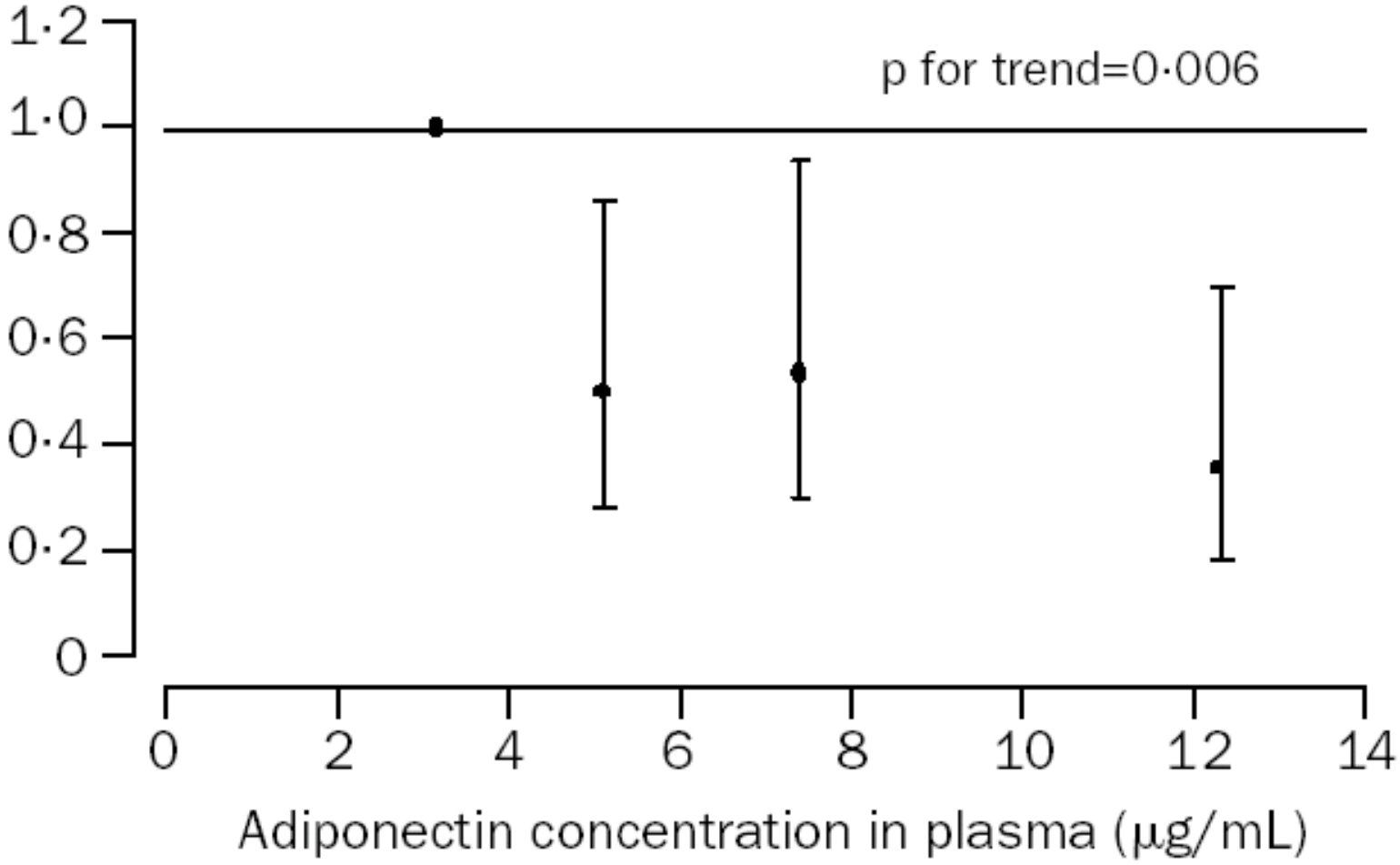
Adjusted Relative Odds of Incident Diabetes in 1500 Women by CRP Quintile and Weekly ASA Use: Nurses Health Study (Nested Case-Control)



FB Hu et al.
***Diabetes* 2004;**
53:693-700

Adjusted for age, race, BMI, smoking, physical activity, family hx, HRT, & Diet

Relative Odds of Incident Type 2 Diabetes in a Nested Case-Control Study of 576 Europeans by Baseline Plasma Adiponection: The EPIC Study



J Spranger et al. Lancet 2003; 361:226-28

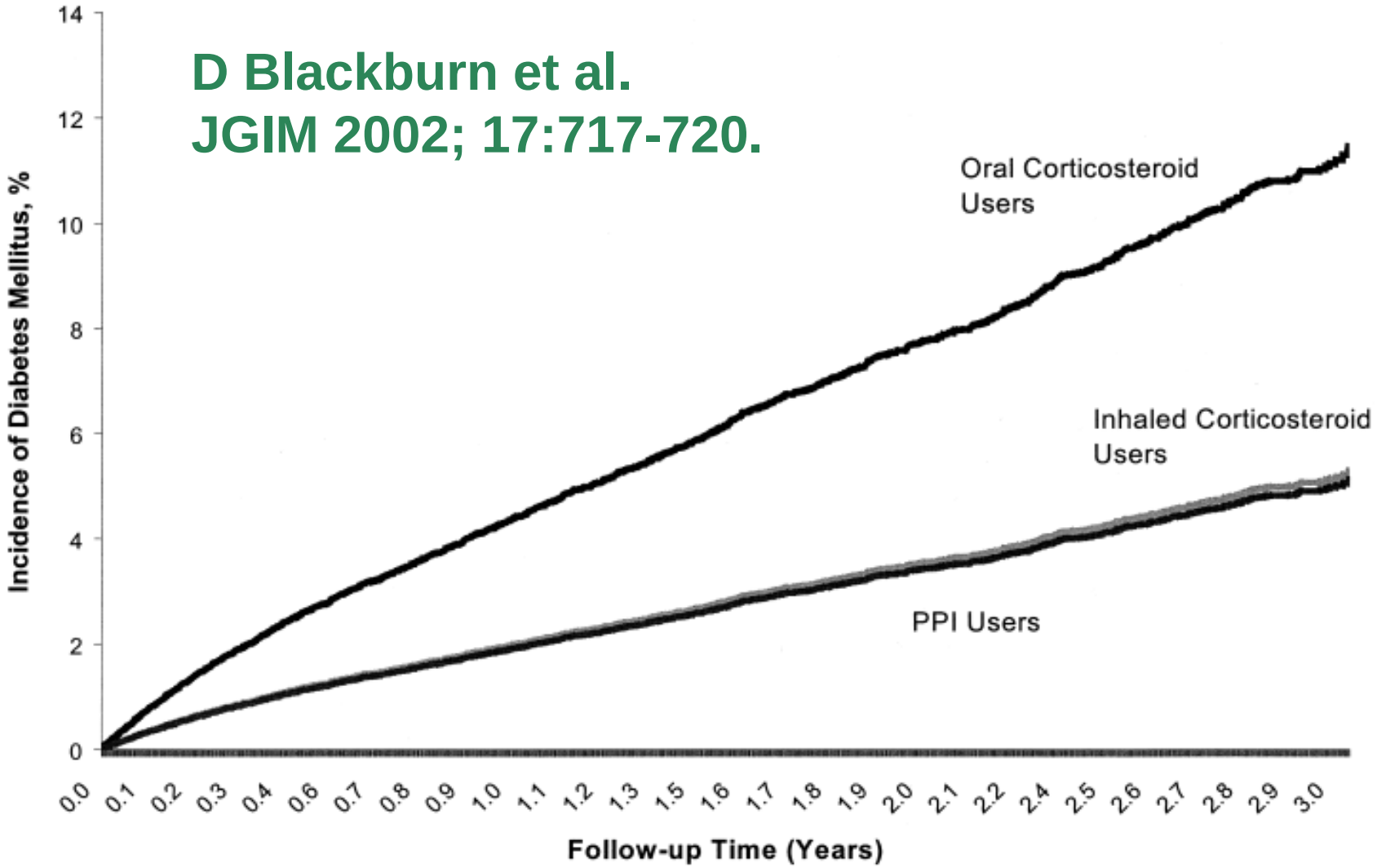
Relative Hazard (95%CI) of Incident Diabetes in 1230 HIV-infected Adults During first Treatment with Highly Active Retroviral Therapy

Characteristic	Unadjusted	Fully Adjusted
NNRTI	1 (ref)	1 (ref)
PI	2.8 (1.0–8.0)	5.0 (1.4–18.2)
NNRTI + PI	2.0 (0.5–8.0)	3.3 (0.7–16.2)
HCV positive	2.1 (1.2–3.8)	2.3 (1.2– 4.2)
Age (per 10 yr)	1.4 (1.0–1.8)	1.4 (1.0– 1.8)

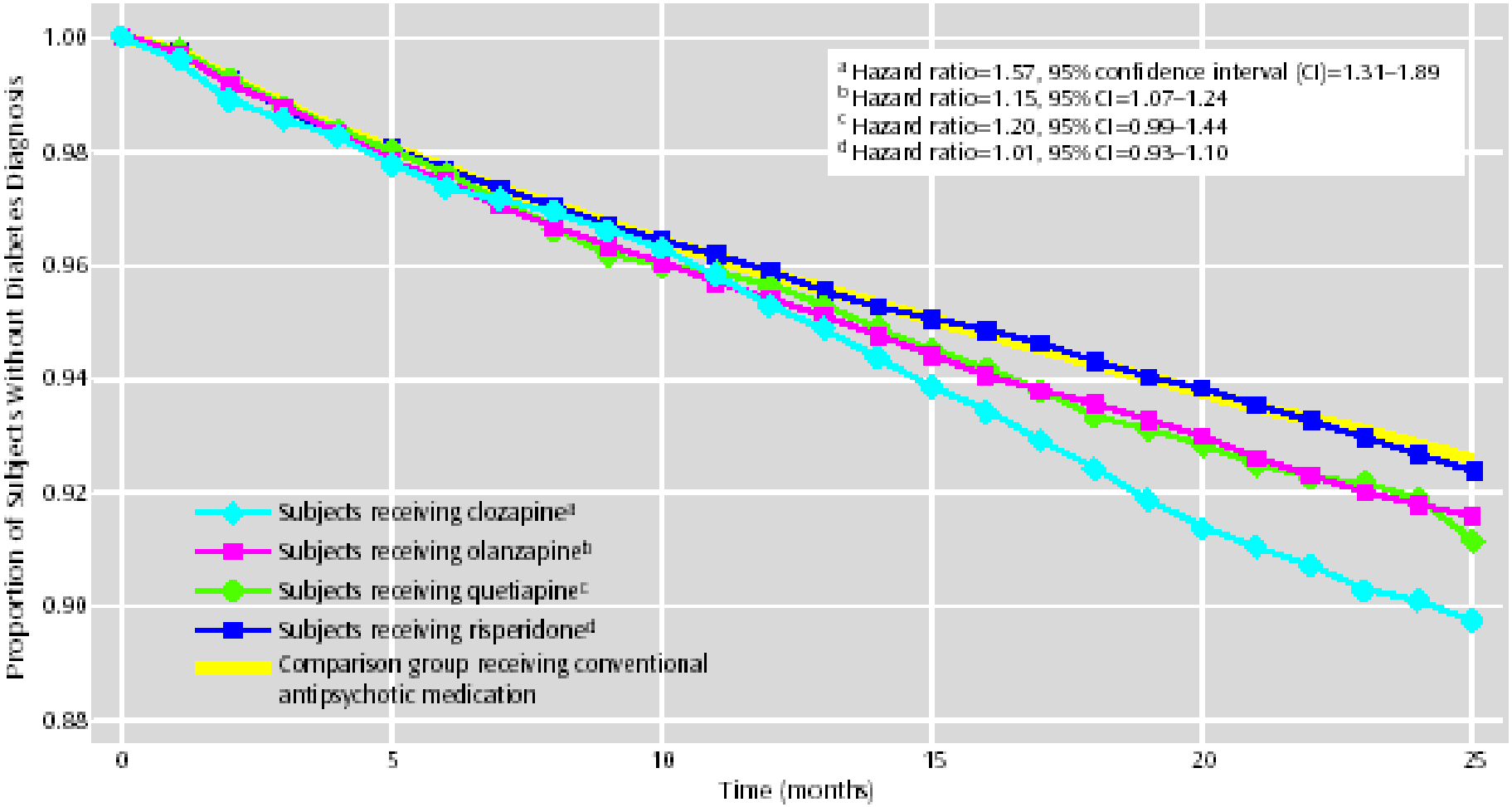
NNRTI = non-nucleoside retroviral transcriptase inhibitor; PI = protease inhibitor

SH Mehta et al. J Acquir Immune Defic Syndr. 2003 Aug 15;33(5):577-84

Cumulative Incidence of Diabetes in a Pharmacy Database of 122,000 Ontario Seniors Using Oral Steroids, Inhaled Steroids, or PPIs (Control Group)

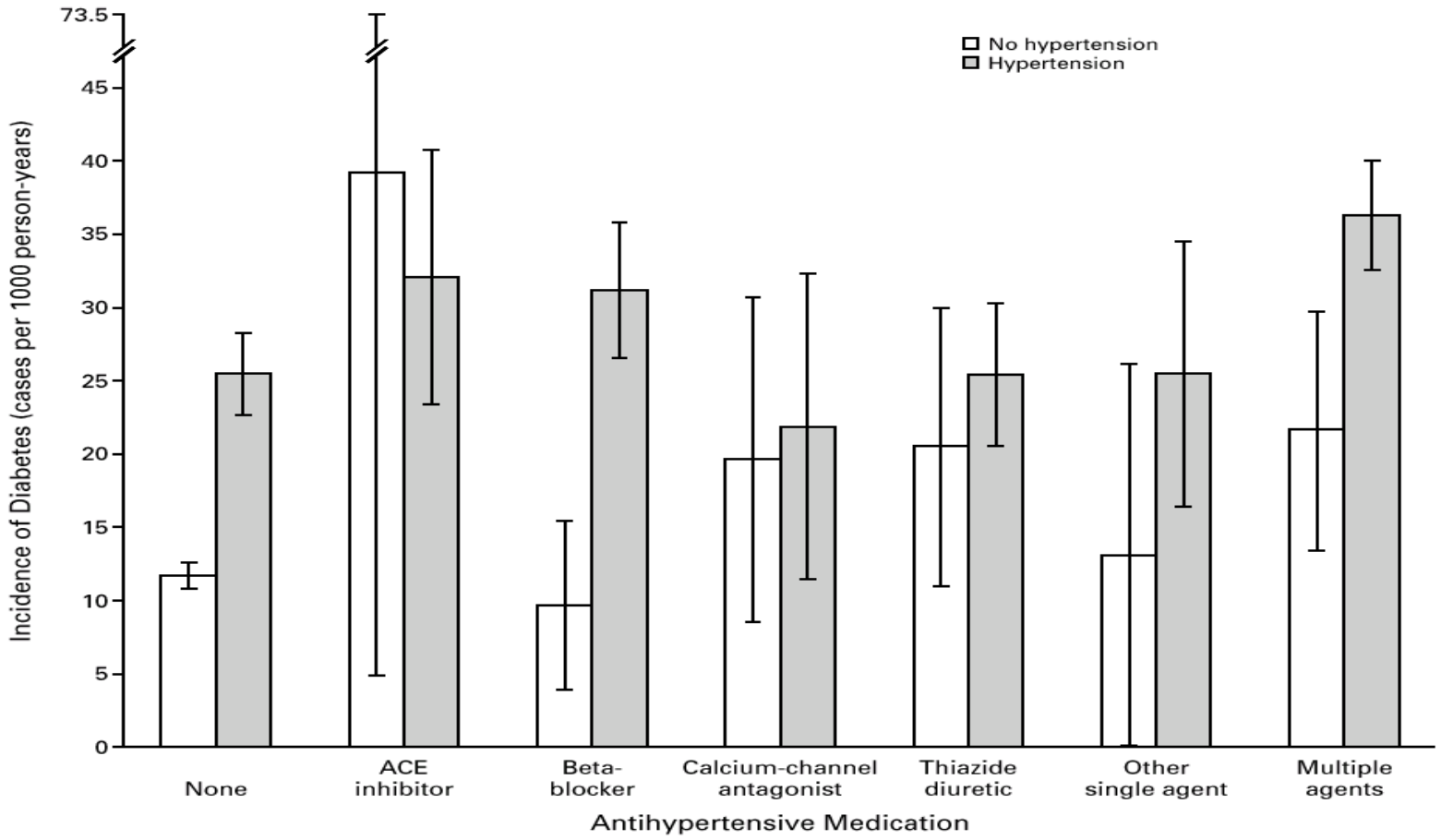


Diabetes-Free Survival in 56,849 VA Patients with Schizophrenia By Type of Antipsychotic Medication Used



DL Leslie et al. Am J Psychiatry 2004; 161:1709–1711)

Incidence of Type 2 Diabetes in 12,550 Middle-Aged Adults by Hypertension Status & Use of Anti-Hypertensive Drugs



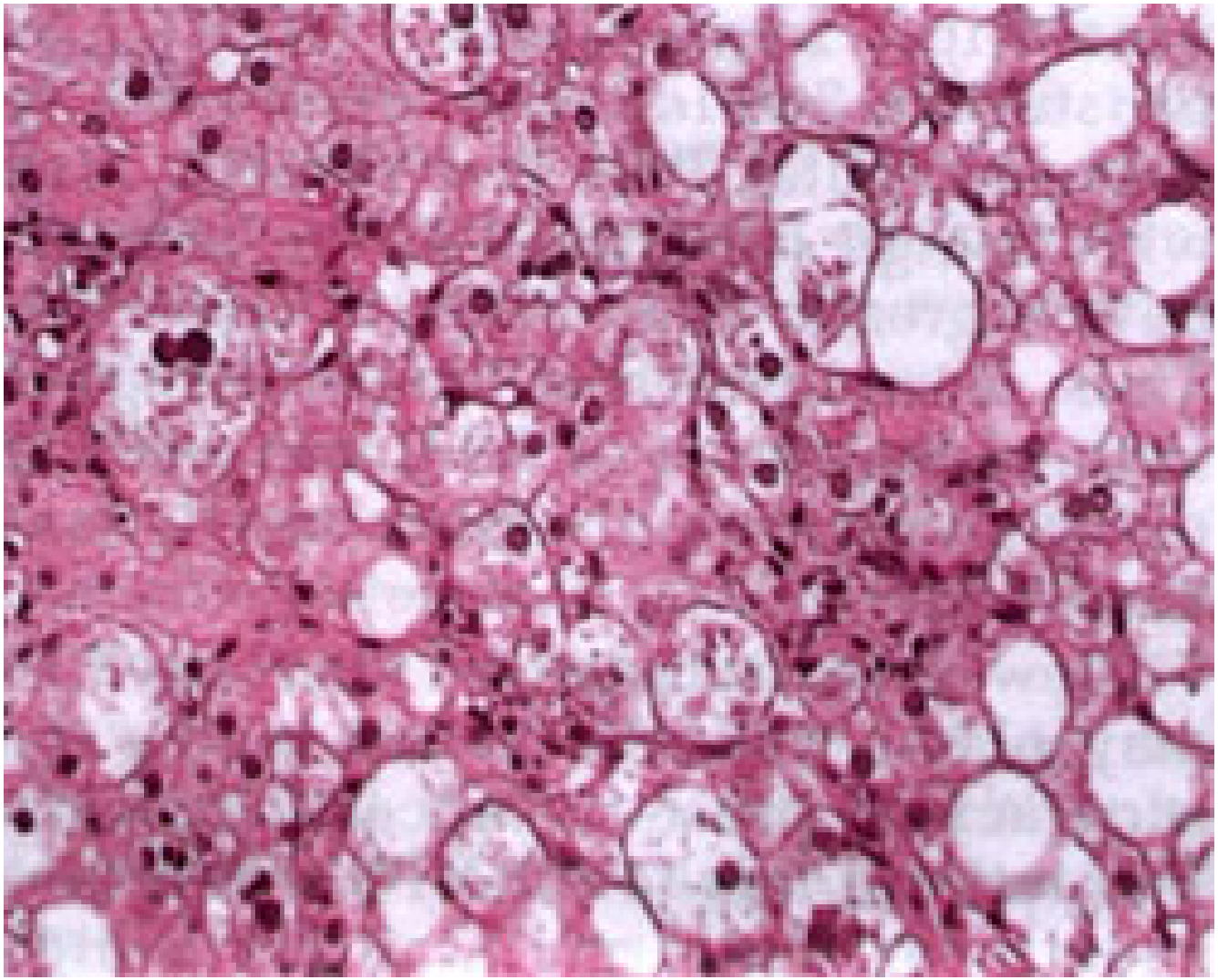
T Gress et al. N Engl J Med 2000; 342:905-12.

Adjusted Relative Risk of Type 2 Diabetes in 3804 Middle-Aged Adults with Hypertension by Type of Anti-Hypertensive Medication Used

Antihypertensive Medication	Hazard Ratio (95% Confidence Interval)		
	Model 1	Model 2	Model 3
None	1.0	1.0	1.0
ACE inhibitor	0.99 (0.73–1.35)	0.96 (0.71–1.31)	0.98 (0.72–1.34)
Beta-blocker	1.26 (1.03–1.52)†	1.25 (1.03–1.52)†	1.28 (1.04–1.57)†
Calcium-channel antagonist	1.17 (0.85–1.62)	1.16 (0.84–1.60)	1.17 (0.83–1.66)
Thiazide diuretic	0.95 (0.77–1.17)	0.93 (0.76–1.15)	0.91 (0.73–1.13)

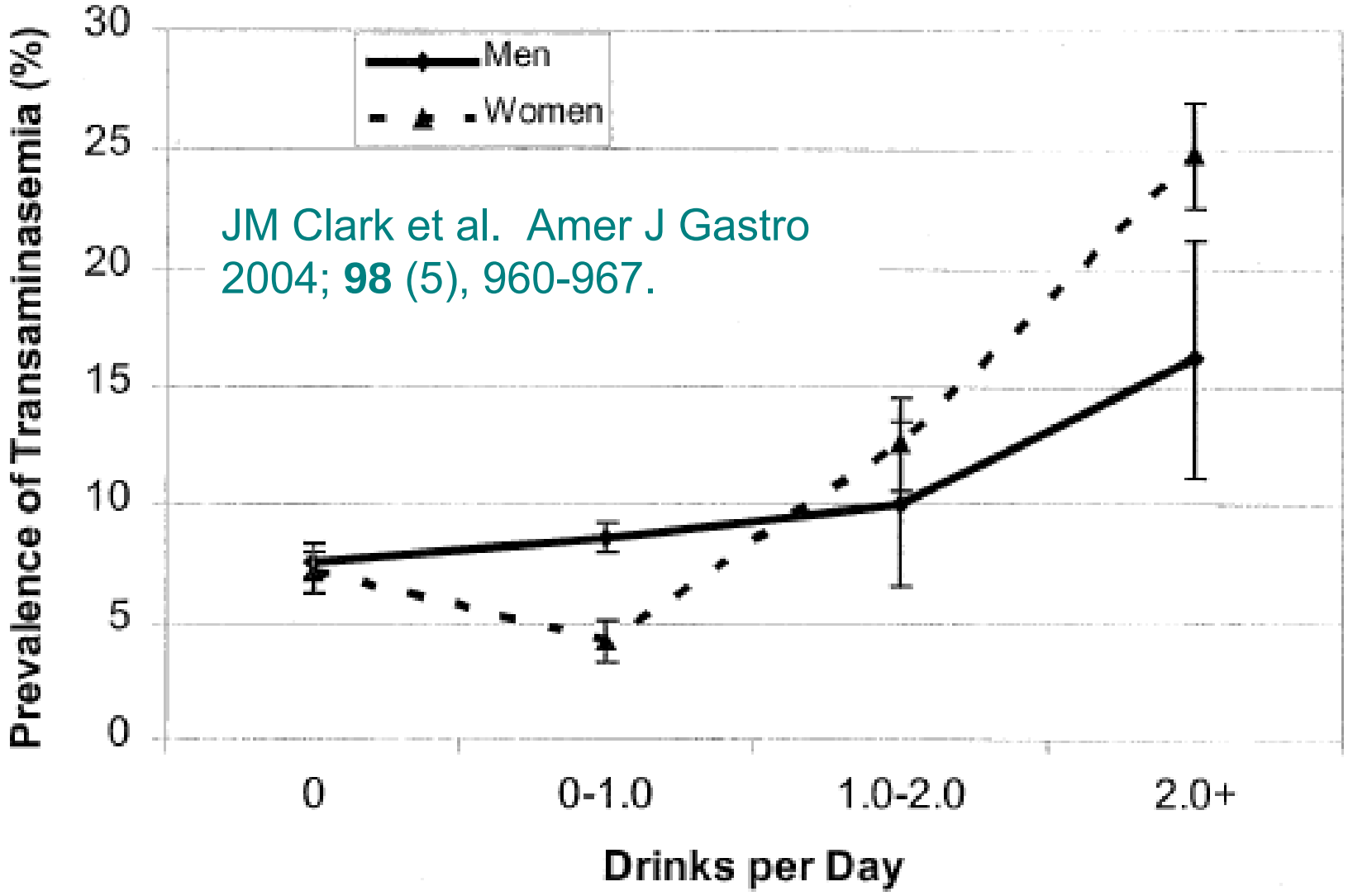
*Model 1 adjusted for age, sex, race, and use of other drugs. Model 2 is further adjusted for BMI,WHR, education, smoking, alcohol use, and physical activity. Model 3 is further adjusted for systolic BP, diastolic BP, fasting insulin, family history of diabetes, and history of selected comorbid conditions (e.g. CVD, renal disease, COPD, asthma).

T Gress et al. N Engl J Med 2000; 342: 906-12.



Steatohepatitis. The histologic findings shown include macrovesicular steatosis, cytologic ballooning, Mallory bodies, and scattered lobular inflammation.

Prevalence of Elevated Aminotransferases By Sex & Number of Alcoholic Drinks US Adults, NHANESIII

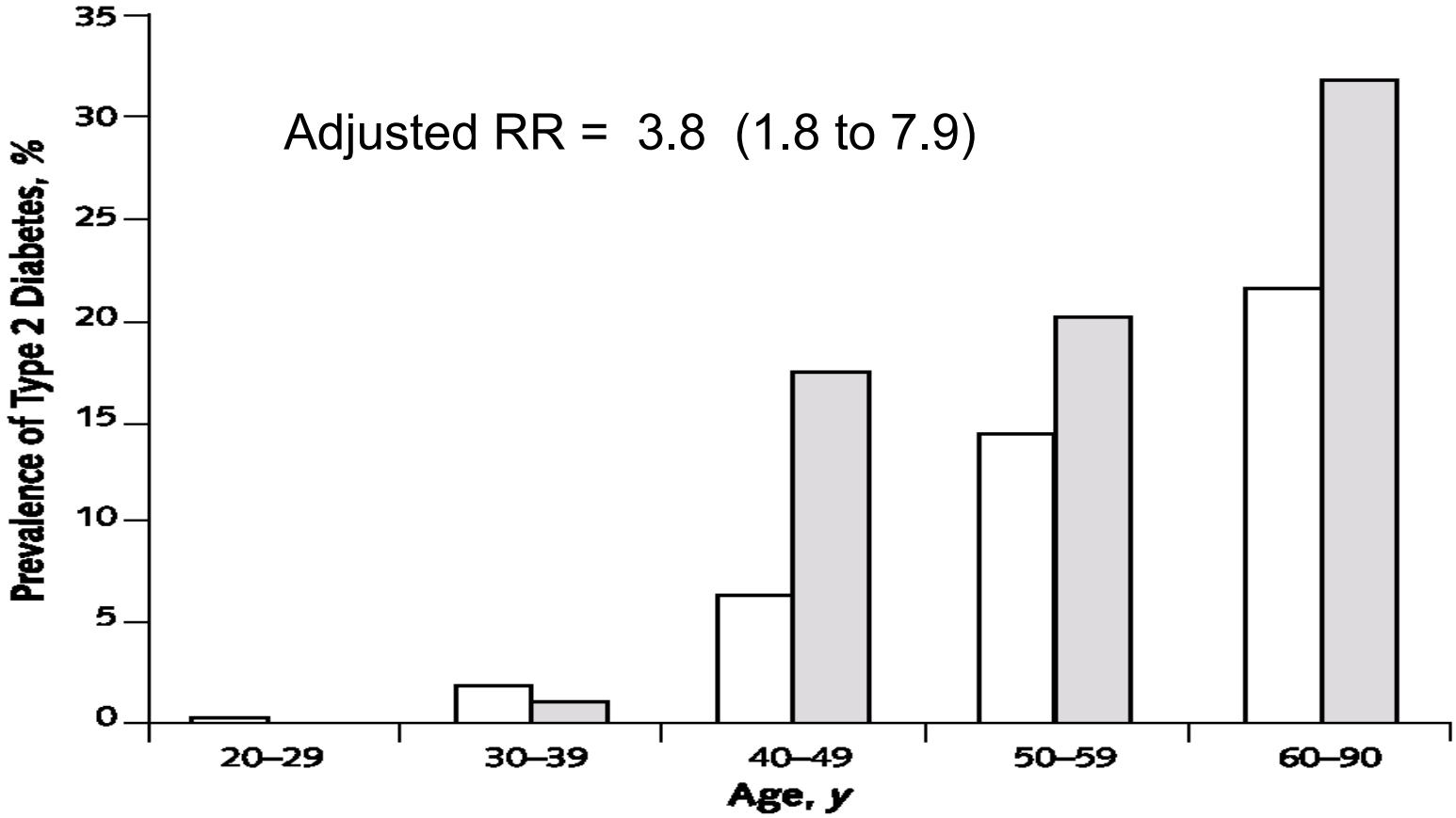


Selected Metabolic Characteristics of by Amino-transferase Status in a Representative Sample of US Women, Aged 40-74, NHANESIII

Characteristic	Women		
	Normal	Explained Aminotransferase Elevation	Unexplained Aminotransferase Elevation
Body mass index (kg/m^2)	26.2 (0.2)	28.0 (1.4)	29.1 (0.5)*
Waist circumference (cm)	87.7 (0.4)	94.5 (3.1)	95.8 (1.3)*
Total cholesterol (mmol/L)	5.27 (0.02)	5.28 (0.16)	5.54 (0.08)*
Fasting triglyceride (mmol/L)	1.37 (0.03)	1.82 (0.18)	2.14 (0.16)*
HDL cholesterol (mmol/L)	1.43 (0.01)	1.48 (0.05)	1.30 (0.04)*†
Fasting glucose (mmol/L)	5.27 (0.03)	5.72 (0.25)	6.06 (0.27)*
Fasting insulin (pmol/L)	58 (1)	105 (21)	95 (5)*
Insulin resistance (HOMA)	2.94 (0.11)	3.51 (0.74)	3.33 (0.64)
Exercise (MET)	86.5 (3.3)	85.1 (9.9)	80.2 (9.0)
HbA_{1c} (%)	5.3 (0.0)	5.1 (0.1)	5.9 (0.1)*†
Type 2 diabetes (%)	5.2 (0.4)	13.5 (4.7)	16.0 (2.7)‡
Hypertension (%)	22.9 (0.7)	38.4 (7.9)	32.2 (3.7)‡

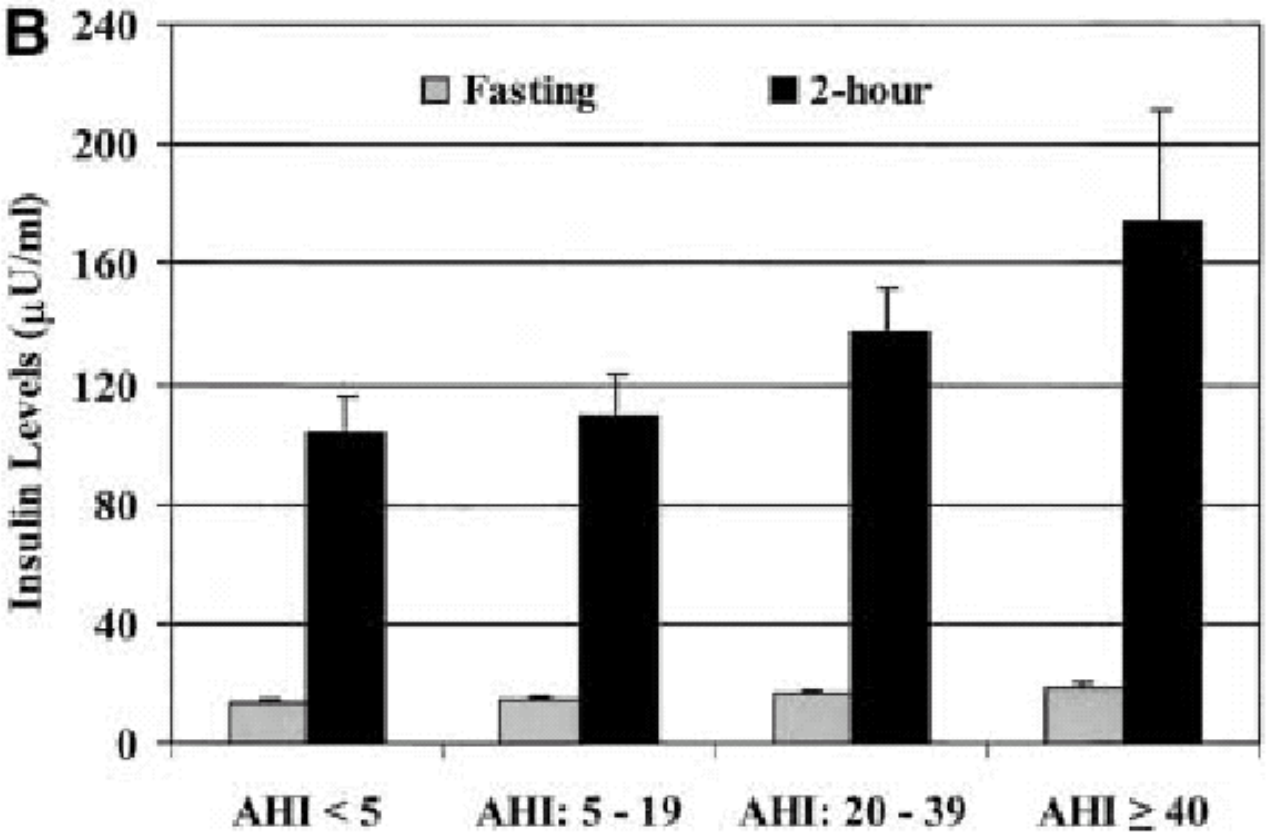
JM Clark et al. Amer J Gastro 2004; **98** (5), 960-967.

Prevalence of Type 2 Diabetes in U.S. Adults by Age and Hepatitis C Antibody Status: NHANESIII



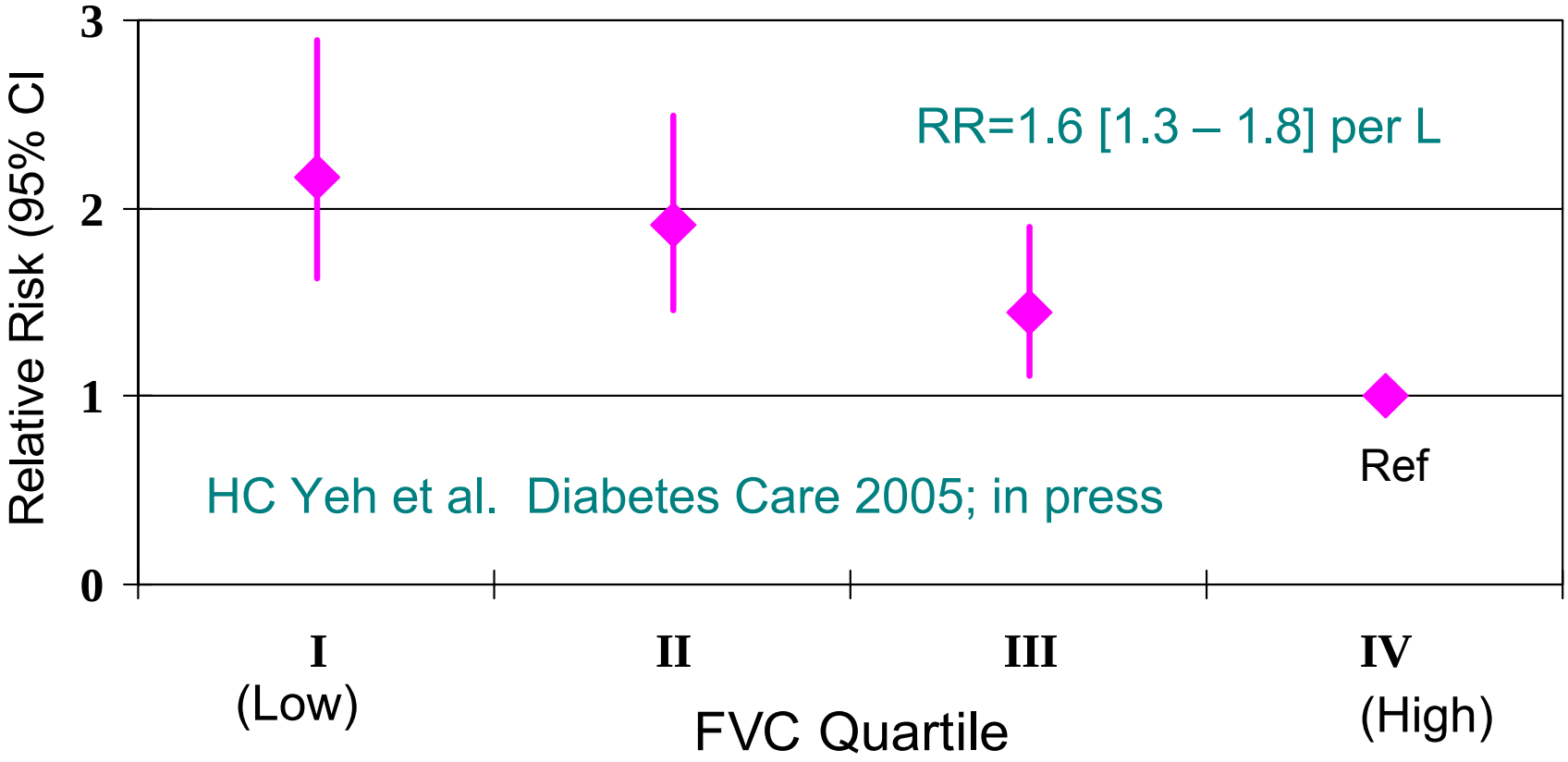
S Mehta et al. Ann Intern Med 2000; 133: 592-99.

Fasting and 2-hr Insulin Levels by Apnea-Hypopnea Index (AHI) in 150 Overweight Adults Aged 45 and Older



NM Punjabi et al. Am J Respir Crit Care Med 2001; 165:677-82.

9-yr Relative Hazard§ for Incident Diabetes in 7,504 Middle-Aged Women by FVC Quartile at Baseline: The ARIC Study



§ Adjusted for age, race, height, BMI, pack-years of smoking, lung disease, education, family history, WHR, and sports index

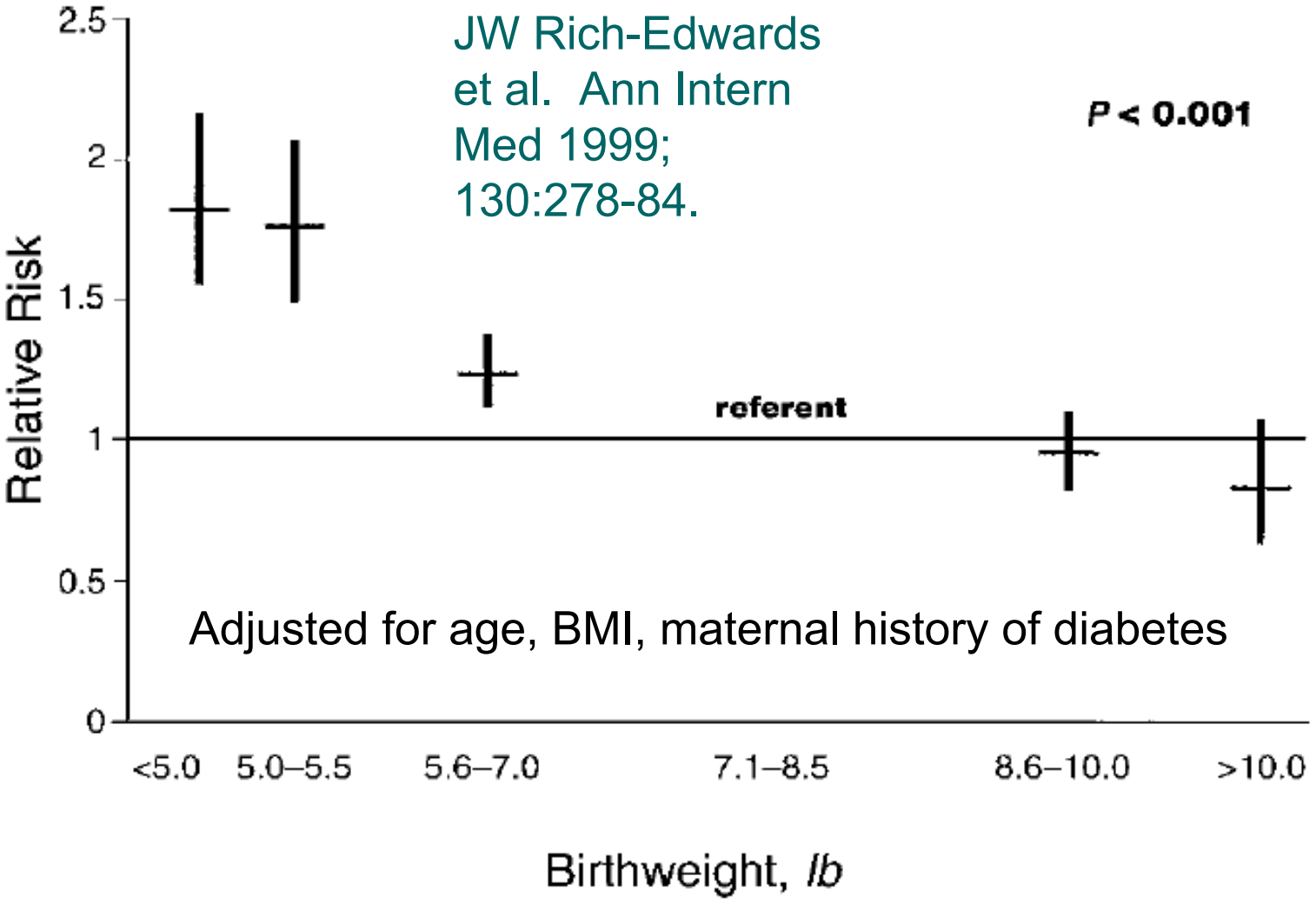
Relative Prevalence of Impaired Glucose Tolerance (IGT) and Type 2 Diabetes in US Adults by Upper Leg Length: NHANESIII

Model	Prevalence Ratio (per 10 cm decline; 95%CI)	
	IGT	Type 2 Diabetes
Unadjusted	2.2 (1.5, 3.1)	3.7 (2.6, 5.7)
Age, Sex, Ethnicity	1.8 (1.1, 2.8)	4.8 (2.8, 8.6)
Fully Adjusted †	1.5 (1.0, 2.3)	3.1 (2.0, 4.9)

† adjusted for age, sex, ethnicity, income, education, body-mass index, family history of diabetes, physical activity, and smoking

K Asao et al. Presented at AHA Epidemiology Sessions, 2003.

Adjusted Relative Risk (95%CI) of Incident Type 2 Diabetes by Self-Reported Birth Weight in 121,701 US Women: The Nurses Health Study

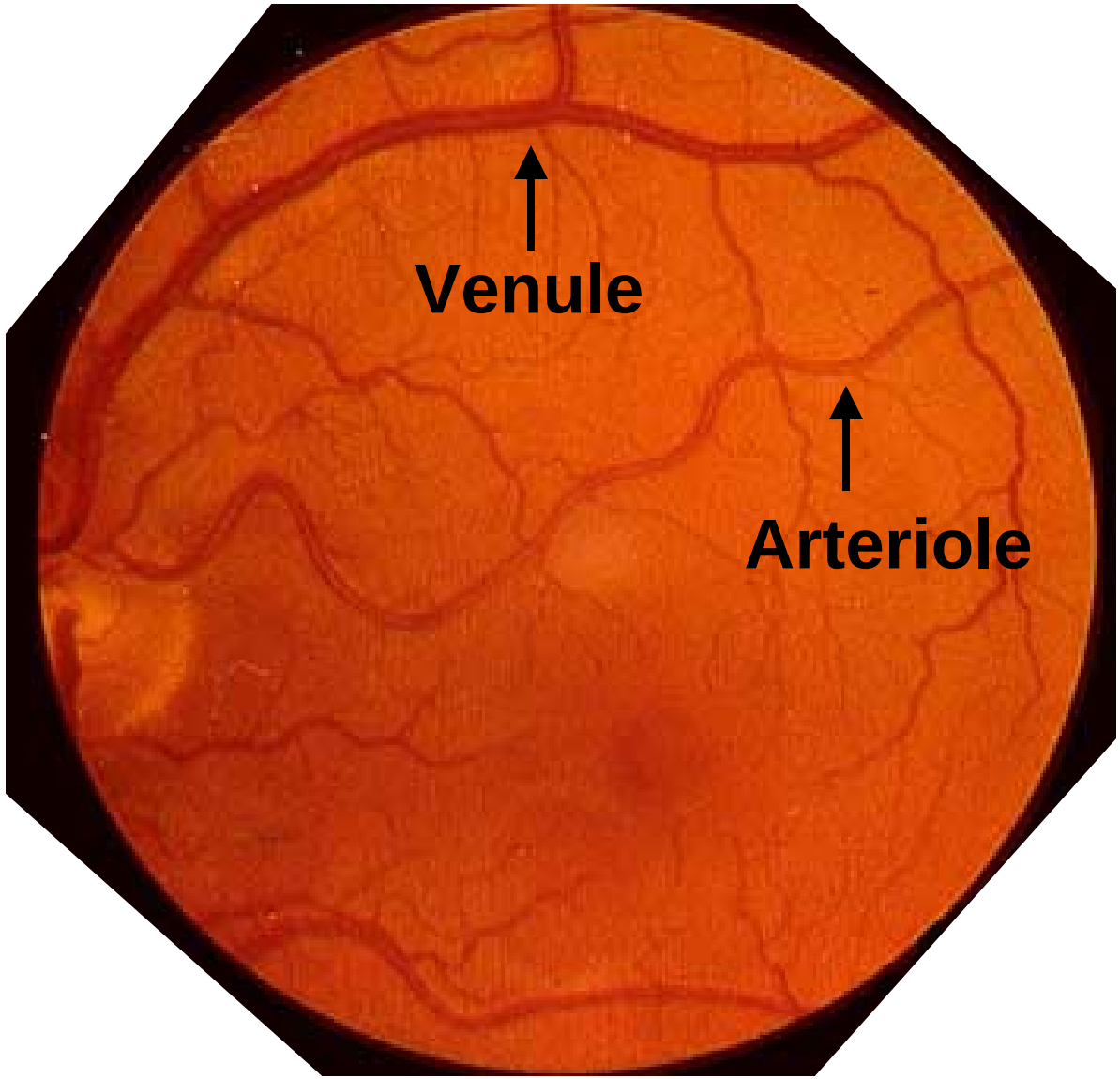


Selected Components of the Insulin Resistance Syndrome in 627 Chinese Adults (mid-40s) by Weight on Birth Certificates

Variable	Birthweight			
	≤2.5 kg	>2.5 to ≤3.0 kg	>3.0 to ≤3.5 kg	>3.5 kg
Participants, *n*	44	184	284	115
Systolic blood pressure, *mm Hg*	128	125	125	122
Diastolic blood pressure, *mm Hg*	79	75	76	74
Fasting glucose level, *mmol/L (mg/dL)*‡	5.7 (103)	5.5 (99)	5.3 (95)	5.2 (94)
2-hour glucose level, *mmol/L (mg/dL)*‡	7.9 (142)	7.1 (128)	6.3 (113)	6.1 (110)
Fasting insulin level, *pmol/L*‡	46	47	44	33
2-hour insulin level, *pmol/L*‡	317	314	218	201
Triglyceride level, *mmol/L (mg/dL)*‡	1.77 (157)	1.38 (122)	1.23 (109)	1.02 (90)
Total cholesterol level, *mmol/L (mg/dL)*	5.15 (199)	4.93 (191)	4.98 (193)	4.84 (187)
LDL cholesterol level, *mmol/L (mg/dL)*	3.05 (118)	2.93 (113)	2.93 (113)	2.83 (110)
HDL cholesterol level, *mmol/L (mg/dL)*	1.35 (52)	1.33 (51)	1.38 (53)	1.41 (55)

J Mi et al. Ann Intern Med 2000; 132:253-260.

Advanced arteriolar narrowing, quantifiable as an arteriole-to-venule ratio of 1:2 or 0.5.



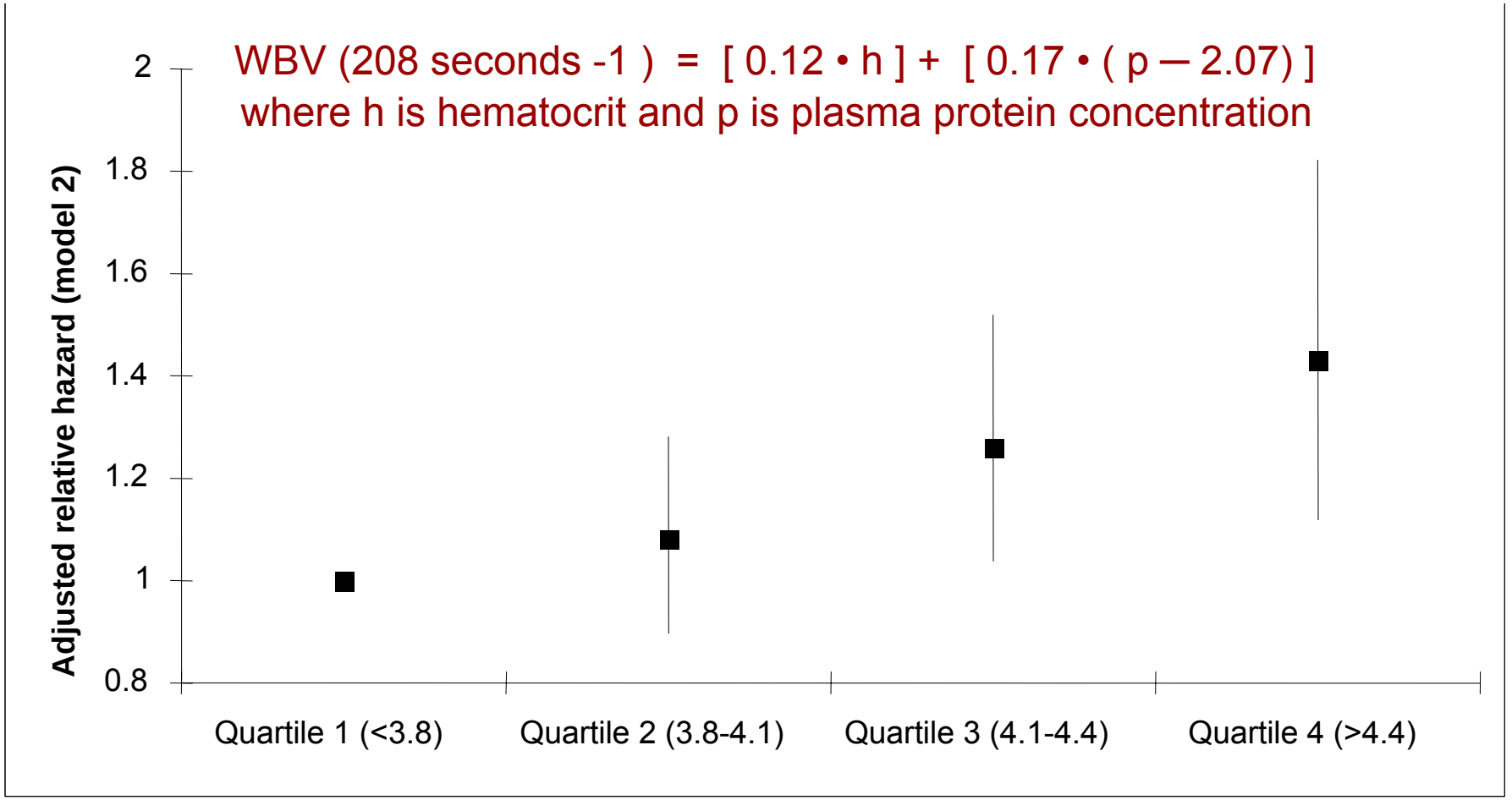
Adjusted Relative Odds of Incident Type 2 Diabetes in 7993 Adults Aged 49-73 by Quartile of Arteriole-to-Venule Ratio: The ARIC Study

Quartile	Rel Odds	95% CI
1st Q [0.57-0.79]	1.71	(1.13, 2.57)
2nd Q [0.80-0.84]	1.49	(0.98, 2.27)
3rd Q [0.85-0.90]	1.22	(0.79, 1.88)
4th Q [0.91-1.22]	1.0	Reference

Adjusted for age, sex, race, field center, glucose, insulin, family history, 6-yr mean BP, BMI, WHR, physical activity, education, smoking, alcohol, lipids

TY Wong et al. JAMA 2002; 287:2528-2533.

Adjusted Relative Hazard of Incident Type 2 Diabetes in 12,000 Middle-Aged Adults by Estimated Whole Blood Viscosity (WBV): The ARIC Study



L Tamariz et al. 2003. Presented at ADA